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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,963	06/28/2002	Erwin Bischoff	Le A 33 965	4889

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,963	BISCHOFF ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-10 and 12-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10 and 12-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 19, 2004 has been entered.

Action Summary

Claims 1, 5, 7-10, 12-18 and 20-26 of record rejected under 35 U.S.C. 103 (a) over Liao et al. (U.S.Patent No. 6,147,109) in view of Niewohner et al. (WO 99/24433) of record is maintained for the reasons stated in the previous office action.

Claims 6 and 19 of record rejected under 35 U.S.C. 103 (a) over Liao et al. (U.S.Patent No. 6,147,109) in view of Niewohner et al. (WO 99/24433) of record and further in view of Doherty, Jr. et al. (U.S.Patent No. 6,037,346) is maintained for the reasons stated in the previous office action.

Claims 1,5,7-10 and 12-18, 20-26 of record rejected under 35 U.S.C. 103 (a) over Liao et al. (U.S.Patent No. 6,147,109) in view of R&D Drug News (1998) is maintained for the reasons stated in the previous office action.

Claims 6-19 of record rejected under 35 U.S.C. 103 (a) over Liao et al. (U.S.Patent No. 6,147,109) in view of R&D Drug News (1998) in view of R&D Drug News (1998) and further in view of Doherty, Jr. et al. (U.S.Patent No. 6,037,346) is maintained for the reasons stated in the previous office action.

Response to Arguments

Applicants' arguments filed November 19, 2004 have been fully considered but they are not persuasive. Applicants essentially argue that Liao et al. disclose numerous disease indications, numerous HMG-CoA reductase inhibitors and numerous second agents but one skilled in the art would have no idea which disease indication and which combination of HMG-CoA reductase inhibitors and second agents would actually be successful since there is no guidance as to effective dosage, treatment schedules, etc. This is not persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one of ordinary skill in the art to

combine vardenafil in Liao et al's composition because Niewohner et al. teach that Vardenafil is useful for the treatment of erectile dysfunction and because Liao et al. teach the HMG-CoA reductase inhibitors can be coadministered with other agents (i.e. impotence therapy adjunct). One would have been motivated to combine vardenafil, well known for the treatment of sexual dysfunction by Niewohner et al. in Liao et al's composition simultaneously with another agent (i.e. impotence therapy adjunct) to achieve at least expected additive benefit in treatment of impotence or even synergistic effect as taught by Liao et al. Therefore, there is clear motivation for combining the components flows from their individually known common utility for treating erectile dysfunction (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). One of ordinary skill in the art would expect that the combination of components would treat erectile dysfunction as well. Furthermore, no unobviousness is seen in the effective amount claimed because once the usefulness of a compound is known to treat a condition, it is within the skill of the artisan to determine the optimum dosage amount. Absent any evidence to contrary there would have been a reasonable expectation of successfully treating sexual dysfunction by combining HMG-CoA reductase and Vardenafil, which are individually known to have same effect as taught by the prior art to achieve at least an additive effect.

Applicants next argue that Doherty et al. mentions additional active agents but there is no suggestion to combine PDE inhibitors with HMG-CoA reductase inhibitors. This is not persuasive because Doherty et al. teach the kit for the erectile dysfunction comprising PDE inhibitors as other active agents are well known in the art. Therefore it

would have been obvious to formulate the Liao et al's composition as modified by Niewohner et al. in a kit since PDE inhibitors with other active agents for the treatment of erectile dysfunction in a kit is old and well-known. One would have been motivated to formulate the combination of HMG-CoA reductase and Vardenafil in a kit for the convenience of having the agents in one package. Applicants argue R& D Drug News discloses vardenafil; however, R & D Drug News does not teach or suggest the combination of vardenafil and HMG-CoA reductase inhibitors and there is no motivation on the disclosure of R& D Drug News to combine vardenafil and HMG-CoA reductase inhibitors. This is not persuasive because R & D Drug News teaches vardenafil is the phosphodiesterase inhibitor and it has a potential therapy for the erectile dysfunction. This teaching is a clear motivation for combining the components flows from their individually known common utility for treating erectile dysfunction (see In re Kerkhoven, 205 USPQ 1069(CCPPA 1980)). Applicants lastly argue that Liao, et al, R & D Drug News and Doherty et al. fail to teach or suggest the invention as presently claimed. This is not persuasive because Liao et al. teach HMG-CoA reductase inhibitors are useful for the treatment of impotence and it can be combined with other active agents with same effect. R & D reference teaches vardenafil can be use for the very same effect, Doherty et al. teach that "kit" is well-known in the pharmaceutical art comprising PDE inhibitors for the erectile dysfunction therapy. As stated in In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980):

> It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21,

279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). As this court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art.

Therefore, it would have been prima facie obvious to combine HMG-CoA reductase inhibitor and vardenafil conjointly in a (kit) formulation to treat erectile dysfunction. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

In view of the above Office Action of May 19, 2004 is deemed proper and asserted with full force and repeated herein to obviate applicants' claims.

Claim Rejections - 35 USC § 103

Claims 1, 5, 7-10, and 12-18, 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao et al. (U.S.Patent No. 6,147,109) in view of Niewohner et al. (WO 99/24433) of record.

Liao et al. teach that HMG-CoA reductase inhibitor such as simvastatin, pravastatin, fluvastatin, cerivastatin, atorvastatin are useful for the treatment impotence in a subject. (column 9, lines 10-65, claims 15-27, column 3, lines 32-39). Liao et al. also teach that the HMG-C0A reductase inhibitors can be co-administered with a

second agent (impotence therapy adjunct) with a condition treatable by the second agent in an amount effective to treat the condition to enhance the result. (column 5, lines 35-40, column 13, lines 14-65, particularly line 63). Liao et al. teach that the reductase inhibitor is administered simultaneously with the second agent close enough in time whereby the two compounds may exert an additive or even synergistic effect. (column 14 , lines 18-28).

Liao et al. does not expressly teach Vardenafil in the above formulation.

Niewohner et al. teach that the Applicants' active agent, vardenafil (hydrochloride, or trihydrate), inhibits $_c$GMP-metabolising phosphodiesterases and is suitable for use in medicaments of treating erectile dysfunction. (abstract, examples 19, 20, 337, 336).

It would have been obvious to one of ordinary skill in the art to combine vardenafil in Liao et al.'s composition because Niewohner et al. teach that Vardenafil is useful for the treatment of erectile dysfunction and because Liao et al. teach the HMG-CoA reductase inhibitors can be coadministered with other agents (i.e. impotence therapy adjunct). One would have been motivated to combine vardenafil well known for the treatment of sexual dysfunction by Niewohner et al. in Liao et al.'s composition simultaneously with another agent (i.e. impotence therapy adjunct) to achieve expected additive benefit in treatment of impotence or even synergistic effect as taught by Liao et al. Absent any evidence to contrary there would have been a reasonable expectation of successfully treating sexual dysfunction because they are drawn to same technical

fields (constituted with same effect or utility), which are pertinent to the treatment of sexual dysfunction.

Claims 6 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao et al. (U.S.Patent No. 6,147,109) in view of Niewohner et al. (WO 99/24433) of record as applied to claims 1, 5, 7-10, and 12-18, 20-26 above, and further in view of Doherty, Jr. et al. (U.S.Patent No. 6,037,346).

Teachings of Liao et al. and Niewohner et al. as applied as before.

Liao et al. and Niewohner et al. do not expressely teach the kit set forth in claims 6 and 19.

Doherty, Jr. et al. teach the kit for the erectile dysfunction comprising PDE inhibitors and different active agents. (abstract, column 3, lines 20-37,column 14, lines 26-40).

It would have been obvious to formulate the Liao et al.'s composition as modified by Niewohner et al. in a kit because Doherty, Jr. et al. teach that erectile dysfunction treatment of a kit is old and well-known. One would have been motivated to make such a modification for the conveniently treating erectile dysfunction by having the therapeutic agents accessible in one package.

Claims 1, 5, 7-10, and 12-18, 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao et al. (U.S.Patent No. 6,147,109) in view of R&D Drug News (1998).

Liao et al.'s teachings as applied as before.

Liao et al. disclose that salts, esters, amides, prodrugs and other derivatives of the active agents may be prepared using standard procedures known to those skilled in the art of synthetic organic chemistry. (column 8, lines 38-40).

Liao does not expressly teach the vardenafil and its specified salt (i.e. trihydrate).

R&D Drug News teaches vardenafil is the phosphodiesterase inhibitor is in preclinical trials as a potential therapy for erectile dysfunction.

It would have been obvious to one of ordinary skill in the art to combine vardenafil in Liao et al.'s composition because R&D Drug News teaches that Vardenafil is in preclinical trial as a potential therapy for erectile dysfunction and because Liao et al. teach the HMG-CoA reductase inhibitors can be coadministered with other agents (i.e. impotence therapy adjunct). One would have been motivated to combine vardenafil well known for having potential therapy for erectile dysfunction in Liao et al.'s composition simultaneously with HMGCoA reductase inhibitors to achieve expected additive benefit in treatment of impotence or even synergistic effect as taught by Liao et al. Absent any evidence to contrary there would have been a reasonable expectation of successfully treating sexual dysfunction because they are drawn to same technical fields (constituted with same effect or utility) which are pertinent to the treatment of sexual dysfunction. The pharmaceutical salts, e.g., trihydrate, etc; is deemed obvious since they are all within the knowledge of the skilled pharmacologist and that salts, esters, amides, prodrugs and other derivatives of the active agents may be prepared

using standard procedures known to those skilled in the art of synthetic organic chemistry as disclosed by Liao et al.

Claims 6 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liao et al. (U.S.Patent No. 6,147,109) in view of R&D Drug News (1998) as applied to claims 1, 5, 7-10, and 12-18, 20-26 above, and further in view of Doherty, Jr. et al. (U.S.Patent No. 6,037,346).

Teachings of Liao et al. and R&D Drug News (1998) applied as before.

Liao et al. and R&D Drug News do not expressly teach the kit set forth in claims 6 and 19.

Doherty, Jr. et al. teach the kit for the erectile dysfunction comprising PDE inhibitors and different active agents. (abstract, column 3, lines 20-37,column 14, lines 26-40).

It would have been obvious to formulate the Liao et al.'s composition as modified by R&D Drug News in a kit because Doherty, Jr. et al. teach that erectile dysfunction treatment of a kit is old and well-known. One would have been motivated to make such a modification for the conveniently treating erectile dysfunction by having the therapeutic agents accessible in one package.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

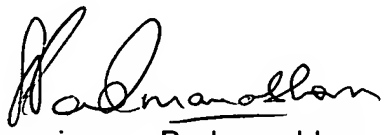
All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
January 28, 2005